REMARKS

Applicants have canceled claim 35 without prejudice. Claims 21, 28, and 36 have been amended solely for greater clarity. Support for the amendments can be found throughout the specification. No new matter has been introduced. Applicants further submit that the amendments and cancellations are made merely to expedite allowance of claims directed to most commercially relevant embodiments of the present invention. Applicants reserve the right to pursue claims of similar or differing scope in the future.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Election/Restriction

The Examiner has acknowledged Applicants' election, with traverse, of Group II (claims 21-36) in the Response filed on May 27, 2005.

Specifically, the Examiner indicates that the "limitation" of applying the measurements in "live" children is not included in the claims (Office Action, page 3, paragraph 1C). Applicants wish to point out to the Examiner that independent claims 20, 21, and 37 all recite "a method of assessing **potential susceptibility** to development of ALTE and/or SIDS" in a subject or an infant. Since the methods specifically refer to "potential susceptibility," the subject or infant is necessarily alive. Accordingly, Applicants request that the Examiner read the limitations into the claims and rejoin withdrawn claims 20 and 37 with elected Group II.

Information Disclosure Statement

The Examiner asserts that the references cited on pages 15 and 16 of the specification have not been incorporated into an Information Disclosure Statement (IDS). Applicants will submit a supplemental Information Disclosure Statement shortly, if necessary.

Oath/Declaration

Applicants enclose herewith a new declaration which has been executed by the inventors, thereby obviating the objection. Applicants note that further amendments to their addresses have been made, initialled, and dated.

Objection to the Specification

First, the Examiner indicates that the specification does not include an abstract. Applicants have amended the specification by adding an abstract.

Second, the Examiner requests that trademarks be capitalized and be accompanied by generic terminology. Applicants have amended the specification to obviate the objection.

Third, the Examiner objects to the disclosure because of three informalities. Applicants have amended the specification to: (a) remove one of the two periods at the end of page 2, line 20; (b) remove reference to Appendix C; and (c) renumber Table 1 on page 13 as Table 4.

Claim Objections

The Examiner objects to claims 21 and 28 due to the use of the acronyms ALTE, SIDS, and ELISA. Applicants have amended claims 21 and 28 to include the definitions of these abbreviations, thereby obviating the objections.

Claim Rejections – 35 USC 112, 2nd Paragraph

The Examiner rejects claims 23, 30, 34, 35, and 36 on the basis that they are indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Applicants respectfully disagree and contend that all the terms objected to by the Examiner are well known and understood in the art.

A. The Examiner alleges that in claim 23 symptoms of URTI are vague and indefinite and questions whether the sample will be collected after URTI and what the symptom of URTI is. Applicants submit that claim 23 clearly recites that the sample "is a sample from a subject at the time of, or any time up to approximately 2 weeks after, an upper respiratory tract infection (URTI) and/or symptoms." As such, the time at which the sample is collected is sufficiently clear to one of skill in the art. Further, what constitutes symptoms of a URTI was abundantly clear to a skilled artisan at the time this application was filed. Indeed, such symptoms were commonly known in the community at large, such as sneezing, coughing, sore throat, insomnia, irritability, and elevated temperature.

B. The Examiner alleges that the term "rapid near-subject assay" in claim 30 is vague and indefinite. Applicants submit that this term was well understood in the art at the time this application was filed. One of skill in the art would readily know that a rapid near-subject assay

is one that does not have to be performed at a specialized clinic or laboratory, i.e., no specialized laboratory skills are required to carry out the assay.

C. The Examiner alleges that claim 34 is vague and indefinite in reciting "an internal personal standard." Applicants submit that this term was well understood in the art at the time this application was filed. One of skill in the art would readily know that an "internal personal standard" is one that is normalized against the tested subject, i.e., samples from the same subject are compared at different time points.

D. The Examiner alleges that claims 35 and 36 are vague and indefinite in reciting "other indices" because it is not clear what other materials Applicant intends to encompass. Solely to expedite prosecution of the application, Applicants have cancelled claim 35 without prejudice and amended claim 36 to recite "[a] method according to claim 21, further including comparison of the ratio of immunoglobulin level to indicators relating to any one or more of: IgM, IgG and acute phase reactants."

Applicants submit that the phrase "acute phase reactants" was well understood in the art at the time this application was filed. For example, it was well known that several proteins in the blood respond to acute infection and are commonly referred to as "acute phase reactants." They include, for example, C-reactive protein. Indicators relating to acute phase reactants, therefore, include parameters such as measurement of C-reactive protein levels and eosinophil sedimentation rate. One of skill in the art would be very familiar with this terminology and would have no difficulty in interpreting the scope of the claim.

In view of the above amendments and remarks, the Examiner is respectfully requested to reconsider and withdraw all rejections under 35 U.S.C. 112, second paragraph.

Claim Rejections – 35 USC 102 (b)

The Examiner has rejected claims 21, 22, 24, 25, 26, 27, 28, 33, 34, 35, and 36 under 35 USC 102(b) as being allegedly anticipated by Friedman et al. (Clinical and Experimental Immunology, 1996, 103(2):206-211). Applicants respectfully traverse this rejection.

The standard for anticipating a claim is clearly outlined in MPEP 2131, and this standard is further supported by the Courts. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art

reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1978). "The identical invention must be shown in as complete detail as is contained in the claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Applicants contend that Friedman et al. fail to satisfy this criteria for anticipating the present invention. In the first instance, Friedman et al. disclose a study of infants immunized against rotavirus. While certainly some infants die of rotavirus, Friedman et al. are not directed in any way to the teaching of methods of assessing potential susceptibility to ALTE and/or SIDS as are presently claimed. In fact, Friedman et al. are concerned with measurement of a normal response to infection with rotavirus (and many other types of infectious organisms) i.e., elevated levels of IgA subclasses. In contrast, the present application is concerned with detecting IgA (IgA1 in claims 21 to 36) such that in cases in which there is an abnormal response to infection in terms of the level of the immunoglobulin, a prediction of the susceptibility of developing ALTE and/or SIDS can be made.

More specifically, the Examiner asserts that "[a]lthough the reference is silent with respect to ALTEs and SIDS this is deemed and [sic] inherent property because the disorders are taught to include dysregulation of mucosal immunity. The specification teaches that ALTEs and SIDS are involved in mucosal immunity . . . In this study IgA1 was shown to be expressed early in infant development and useful in detecting retrovirus antibody activity in infants." See Office Action, page 8, lines 5-17.

Applicants respectfully disagree. MPEP 2112 clearly points out that "[t]he fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic."

> "In re Rijckaert, 9 F.3d 1531, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); In re Oelrich, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. **Inherency, however, may not be established by probabilities or possibilities** (emphasis added). The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' In re Robertson, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-1951 (Fed Cir. 1999)

(The claims were drawn to a disposable diaper having three fastening elements. The reference disclosed two fastening elements that could perform the same function as the three fastening elements in the claims. The court construed the claims to require three separate elements and held that the reference did not disclose a separate third fastening element, either expressly or inherently.)" **MPEP 2112**

Applicants point out that Friedman et al. are directed to a method of measuring a normal increase in IgA levels, which is not a "dysregulation" but rather the infant's natural defence mechanisms at work. In contrast, the inventors of the present invention found that development of ALTE and/or SIDS is, at least in part, the result of an abnormal response, i.e., a true "dysregulation" of the "normal" reaction to infection. This dysregulation results in abnormally high levels of IgA (IgA1) in the infant and these can be measured in order to assess the potential susceptibility of the infant to ALTE and/or SIDS. One of ordinary skill in the art would readily appreciate that ALTE and/or SIDS are **not necessarily** present in Friedman's disorders and thus do not constitute an inherent property of Friedman's disorders.

Although Friedman et al. show that IgA1 was expressed early in infant development and useful in detecting retrovirus antibody activity in infants, Friedman et al. provide no indication that IgA1 can be used as a predictor of ALTE and/or SIDS. Moreover, Friedman et al. are completely silent on assessment of potential susceptibility to development of ALTE and/or SIDS. Accordingly, one of skill in the art has no way of knowing whether IgA1 can be used as a predictor of ALTE and/or SIDS.

In view of the above, Applicants respectfully submit that Friedman et al. fail to meet the limitations of the present claims and thus fail to anticipate the claimed subject matter in independent claim 21. For the same reasons, all claims depending from claim 21 are novel over Friedman et al. Reconsideration and withdrawal of this rejection are requested.

Claim Rejections – 35 USC 103(a)

Claims 23 and 29 are rejected as being unpatentable over Friedman et al. in view of Gleeson et al. (Pediatric Research, 193, Vol 33, no.6, pages 554-556). Claims 30-32 are rejected as being unpatentable over Friedman et al. in view of Rylatt et al. (WO 97/09620). Applicants respectfully traverse these rejections.

As an initial matter, Applicants note that the document attached to the Office Action was a Gleeson reference: Scandinavian Journal of Immunology (1991) 33, 533-541. However, from the specific pages referred to by the Examiner, the relevant citation should be the publication in Pediatric Research. Clarification is respectfully requested.

Pursuant to MPEP 2143 and in view of *In re* Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991), "[t]o establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations."

Applicants have presented the arguments above that Friedman et al. do not teach all the elements of the claimed invention, including, but not limited to, use of IgA1 as a predictor of ALTE and/or SIDS as recited in claim 21. None of the other cited art (Gleeson et al. or Rylatt et al.) bridges the gap between Friedman et al. and the claimed invention. Thus, the cited art fails to teach or suggest all the claim limitations.

Further, Friedman et al. are not concerned in any way with assessment of potential susceptibility to development of ALTE and/or SIDS. It makes no mention of either of these two conditions. Indeed, there is no data on ALTE or SIDs in Friedman et al. Applicants submit that a skilled artisan in light of Friedman et al. would not be motivated to consider it in conjunction with Gleeson et al. or Rylatt et al. since they relate to entirely different fields of endeavour.

In particular, even if a skilled artisan in search of a method for assessing susceptibility to ALTE and/or SIDS had considered the Gleeson reference (singly or even in conjunction with the Friedman reference), he would have concluded that IgA was not the most useful predictor of ALTE and/of SIDS. Applicants wish to bring the Examiner's attention to Figure 1 of Gleeson et al. It clearly shows that IgM levels were higher in the infant at both an earlier stage (at 6 weeks as opposed to 8 weeks) and at a higher level relative to the 95th percentile (at 8 weeks the IgM levels in the infant were 3-fold higher than those of the 95th percentile level, whereas the IgA levels were less than 2-fold higher than those of the 95th percentile level at the same date). Consequently, the Gleeson reference would not motivate a skilled artisan to use IgA or IgA1 as a

predictor of ALTE and/or SIDS but would rather point a skilled artisan in the direction of IgM. Moreover, since there is no teaching in Friedman et al. in relation to ALTE and/or SIDS, a skilled artisan would be reliant on the information in Gleeson et al. for direction and would clearly be motivated to use IgM in preference to IgA. In addition, there is no indication whatsoever in Gleeson et al. that IgA1 would be a better indicator of susceptibility to ALTE and/or SIDS than IgA (IgA1 levels were not measured). As such, the presently claimed invention provides an entirely unexpected result – one that could not have been predicted from the disclosures of the prior art as cited, either alone or in combination.

Similarly, Rylatt et al. fail to bridge the gap between Friedman et al. and the claimed invention and fail to provide any suggestion or motivation to one of ordinary skill in the art to modify the Friedman reference to arrive at the present invention.

Accordingly, the cited references, singly or in combination, do not render obvious the method as recited in independent claim 21. For the same reasons, all claims depending from claim 21 are non-obvious over the cited references. Accordingly, Applicants respectfully request reconsideration and withdrawal of all rejections under 35 U.S.C. § 103(a).

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. If an additional fee is due, please charge our **Deposit Account No. 18-1945, under Order No. BSWV-P01-002.**

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Respectfully submitted,

By _____

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